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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/997,666

11/15/2001

David Botstein

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7590

07/14/2005

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EXAMINER

DEBERRY, REGINA M

ART UNIT

PAPER NUMBER

1647

DATE MAILED: 07/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/997,666

Applicant(s)

BOTSTEIN ET AL.

Examiner

Regina M. DeBerry

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1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 May 2005.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 119-131 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 119-131 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 15 November 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 23 May 2005 has been entered.

Status of Application, Amendments and/or Claims

The amendment filed 23 May 2005 has been entered in full. Claims 119-131 are under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

35 USC § 101 and Claim Rejections - 35 USC § 112, First Paragraph, Enablement

Claims 119-131 remain rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

Applicant cites *Brenner v. Manson*, *Nelson v. Bowler* and *Cross v. Iizuka*. Applicant states that the case law established that Applicant's statements of utility are usually sufficient, unless such statement of utility is unbelievable on its face. Applicant maintains that to overcome the presumption of truth that an assertion of utility by the Applicant enjoys, the Examiner must establish that it is more likely than not that one of

ordinary skill in the art would doubt the truth of the statement of utility. Applicant argues that absolute predictability is not a requirement. Applicant discusses the Utility Guidelines.

Applicant maintains that the specification provides sufficient disclosure to establish a specific, substantial and credible utility for native polypeptides with 80-99% identity to the PRO1185 polypeptide of SEQ ID NO:401. Applicant argues that the Examiner has not made a *prima facie* case for lack of utility. Applicant asserts that Table 8 explicitly states that PRO1185 is significantly overexpressed in lung adenocarcinoma or colon tumors as compared to the normal control and that PRO1185 polypeptide is useful as a diagnostic marker for the presence of one or more lung adenocarcinoma or colon tumors in which it is significantly overexpressed. Applicant criticizes the Examiner's reliance on Haynes *et al.*, Pennica *et al.* and Konopka *et al.* (all of record). Applicant maintains that for the reasons previously set forth in Applicant's response (16 July 2004), the references do not show that a lack of correlation between (DNA) amplification and elevated mRNA levels in general, exists. Applicant discusses articles submitted in their IDS (22 June 2004; Orntoft, Hyman and Pollack). Applicant argues that the art clearly indicates that if a gene is amplified in cancer, it is more likely than not that the encoded protein will also be expressed at an elevated level. Applicant maintains that the Examiner has not shown that a lack of correlation exists between gene amplification and polypeptide over-expression based on the references submitted. Applicant state that they have demonstrated a utility for the PRO1185 polypeptide as a marker for adenocarcinomas of the lung or colon.

Applicant's arguments have been fully considered but are not deemed persuasive. The question is whether the asserted utility is specific or substantial. The state of the art regarding gene amplification and increased protein levels can be opposing as indicated by the references cited by the Examiner and Applicant. Indeed, given the disclosure in art, such as Pennica *et al.*, Konopka *et al.*, and Haynes *et al.*, that there is not always such a correlation, the skilled artisan would not assume it is so, but would perform the experiment to verify it. There is great unpredictability regarding the nature of the instant invention and the state of the art. Increased copy number of DNA does not provide a readily apparent use for the polypeptide, for which there is no information regarding level of expression, activity or role in cancer. The specification fails to teach that **PRO1185 protein levels increase** (Emphasis added).

The scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

Claims 119-131 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. The basis for this rejection is set forth at pages 3-6 of the previous Office Action (16 September 2004).

Applicant incorporates their response to the rejection under 35 USC 101 in response to the rejection under 35 USC 112, first paragraph. Applicant's arguments

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have been fully considered but are not found to persuasive for the reasons discussed above in the maintained rejection in 35 USC 101.

New Rejection:

35 USC § 112, First Paragraph, Written Description

Claims 119-123 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification provides adequate written description for SEQ ID NO:401. The instant claims are drawn to *native sequence* polypeptides having at least 80%, 85%, 90%, 95% or 99% sequence identity with SEQ ID NO:401. The term native sequence encompasses naturally-occurring truncated or secreted forms, naturally-occurring variant forms and naturally-occurring allelic variants of the PRO polypeptide. None of these sequences meet the written description provision of 35 USC 112, first paragraph. The specification only shows possession of a single species, not naturally-occurring forms or variants. The specification does not place any limit on the number of substitutions, deletions, insertions and/or additions that may be made to SEQ ID NO:401. The specification does not provide any guidance as to what changes should be made and which regions of the instant protein are functionally and structurally critical. There is no description of variants of SEQ ID NO:401 that exist, while still maintaining

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function. Thus, the specification provides insufficient written description to support the genus encompassed by the claim.

The disclosure fails to describe the common attributes or characteristics that identify the members of the genus, and because the genus is variant, SEQ ID NO:401 alone is insufficient to describe the genus. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus.

In addition, the art does not recognize making a variant of a diagnostic marker. The specification states that PRO1185 polypeptide (SEQ ID NO:401) is useful as a diagnostic marker for the presence of lung adenocarcinoma or colon tumors. A variant diagnostic marker is less specific for its target, and the art teaches away from making such. There is no assurance that those variants of the PRO1185 polypeptide would have the desirable properties of the instant invention. A degenerative marker allows for imperfect matches and carry the risk of obtaining false signals from unrelated sequences.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the ‘written description’ inquiry, whatever is now claimed.” (See page 1117.) The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” (See Vas-Cath at page 1116).

With the exception of SEQ ID NO:401, the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides and polynucleotides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Due to the breadth of the claimed genus and lack of the definitive structural or functional features of the claimed genus, one skilled in the art would not recognize from the disclosure that the Applicant was in possession of the claimed genus. Therefore, only isolated polypeptides comprising the amino acid sequence set forth in SEQ ID NO:401, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Conclusion

No claims are allowed.

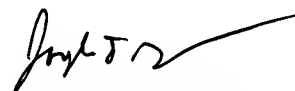
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (571) 272-0882. The examiner can normally be reached on 9:00 a.m.-6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda G. Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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JOSEPH MURPHY
PATENT EXAMINER